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(54) Title of the invention ROOT CANAL TREATMENT AGENT

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SPECIFICATION

1. TITLE OF THE INVENTION

Root Canal Treatment Agent

2. SCOPE OF PATENT CLAIMS

1. A slow-release root canal treatment agent prepared by dispersing 1 or more kinds of active ingredients for the treatment of a root canal in the polymer base formed in a rod-shape or a fiber shape formula with a diameter of 0.05 to 3.0 mm.

2. The root canal treatment agent as described in Claim 1 wherein the active ingredients for the treatment of a root canal are selected from disinfectants, antibacterial agents, analgesics and anti-inflammatory agents.

3. The root canal treatment agent as described in Claim 1 wherein the content of the active ingredients for the treatment of a root canal in the formula ranges from 0.01 to 30 wt%.

4. The root canal treatment agent as described in Claim 1 wherein the polymer base is made of one or more kinds of polymers elected from water-soluble polymers, water-insoluble polymers or barely soluble polymers or polymers that can be dissolved in a limited pH region.

3. DETAILED DESCRIPTION OF THE INVENTION

(FIELD OF INDUSTRIAL APPLICATION)

This invention relates to a root canal treatment agent. More precisely, it relates to a slow-release root canal treatment agent that is inserted in the rod-shape or fiber-shape into the root canal that is capable of maintaining active ingredients in a root canal at an effective concentration by dispersing a disinfectant against the intrathecal bacteria, an antibacterial agent or analgesic anti-inflammatory agent in the polymer bases, wherein the release of the active ingredient is controlled and the potency can be sustained.

(PRIOR ART)

When dental caries are advanced and the dental pulp is exposed and the dental cavity is infected with various oral bacteria. For the treatment of a decayed tooth, generally, the infected root canal is cleaned by extirpation of the dental pulp, a root canal treatment agent is topically applied and then temporarily sealed generally for 2 to 7 days in order to disinfect the root canal, followed by filling the root canal, forming an abutment tooth and installing a cast crown. The root canal treatment agents are used for removal of infection sources such as extermination of bacteria invaded in the wall of the root canal and for treating acute and chronic inflammation of the periodontal tissue. For the former pur-

pose, a topical application of the root canal is performed due to the following three reasons.

(1) Even with complete mechanical removal of infected dental pulp tissue and bacteria, there is no guarantee that the procedure is clinically sufficient.

(2) Even though the dental tubule is exposed in a healthy state, there is no method for determining accurately that there is no bacterial invasion into the dental tubule at the initial stage of infected root canal.

(3) The topical application may play an effective role for the contamination from the entrance of the root canal at the time of root canal treatment procedures.

Next, the following procedures are applied. After cleaning the root canal, the pulp chamber and the root canal are dried using a sterilized cotton ball and a paper point, and a small mount of a topical agent is absorbed in a sterilized cotton ball in order to topically apply the agent only in the pulp chamber. Finally, an extra agent is absorbed by another cotton ball and then temporarily sealed with Cavit, a water-settable sealing material. The agents that are most often used include formalin series agents such as formocresol, phenol camphor, etc. and phenol agents. Since these agents are strongly irritable, one must pay special attention not to adhere them on other parts of the soft tissue in the mouth.

As was mentioned above, currently, formalin series or phenolic series liquid agents are absorbed by sterilized cotton balls in order to apply the agents topically. However, due to strong irritability of these agents, great attention must be paid when performing these procedures. There is also a possibility of causing hypersensitivity reactions. For this reason, there has been a strong demand for a root canal treatment agent with high safety that can be applied by a simple method. Also, it is necessary to have a root canal treatment agent having a slow-releasing effect such that the agent can remain locally at least during the active period.

(PURPOSE AND CONSTITUTION OF THE INVENTION)

Under the aforementioned circumstance, the inventors made efforts for the purpose of maintaining a variety of active ingredients for the treatment of the root canal at effective concentrations during the active period within the root canal as well as developing a simple root canal agent that demonstrates high safety and that can be applied easily. As a result, the aforementioned purpose was found to be achieved by dispersing active ingredients in a substrate which is made of one or more kinds of polymers that are selected from water-soluble polymers, or water-insoluble or barely soluble polymers, or polymers that are dissolved in a limited pH range, and then by forming the dispersion in a rod or fiber form. These findings led us to achieve the present invention.

The formulas concerned in the present invention are manufactured by dispersing one or more kinds of active ingredients in one or more kinds of polymer bases appropriately selected from water-soluble polymers, or water-insoluble or barely soluble polymers or polymers that are dissolved in a limited pH region, and then by forming the dispersion in a solid rod or fiber form.

The polymer bases as dispersion media of the present invention's formulas must form a solid which has physiologically acceptable properties. Among those polymers having such properties, desirable examples are listed below.

The following water-soluble polymers are applicable: methyl cellulose, hydroxypropyl cellulose, sodium carboxy methyl cellulose, hydroxypropyl methyl cellulose, hydroxyl ethyl cellulose, sodium arginate, propylene arginate glycol ester, prulan, tragant, xanthan gum, chitosan, polyethylene oxide, polyvinyl pyrrolidone, polyvinyl alcohol, polyacrylic acid, polymethacrylic acid and their salts, but the desirable polymers are not limited by these examples.

Examples of water-insoluble polymers include ethyl cellulose, acetic acid cellulose, ethyl methacrylate/chlorotrimethylammoniumethyl methacrylate copolymer dimetylaminoethyl methacrylate/methacrylic acid copolymer, polyvinyl acetal/dimethylaminoacetate and cellulose acetate/dibutylhydroxypropylether, etc. Examples of barely soluble polymers include fatty acid polyesters such as polyglycolic acid, polylactic acid, polytetramethylglycolide, polydiethylglycolide, poly epsilon-caprolacton, etc., or their copolymers, but the desirable polymers are not limited by these examples.

Next, polymers that can be dissolved in a limited pH region are described. The pH of the infiltration solution in the root canal is originally a weak alkali, but when intrathecal bacteria have grown, the pH is known to shift to an acidic side. Thus, it is desirable to use polymers that can be dissolved in an acidic side as polymer bases. Examples of polymers that can be dissolved in an acidic side are as fol-

lows: dimethylaminoethyl methacrylate/methylmethacrylate, polyvinyl acetal/dimethylamino acetate, or cellulose acetate/dibutylhydroxypropyloether, but the desirable polymers are not limited by these examples.

As active ingredients that are suitable for a root canal treatment agent of the present invention, any active substances for the treatment of a root canal can be used. Particularly, the following ingredients are desirable: analgesic disinfectants such as formalin, cresol, parafolmaldehyde, clove oil, guaiacol, phenol, parachlorophenol, iodoform, etc. or antibacterial agents such as ampicillin, piperacillin, mecillinam, calpenicillin, cephaloridine, cephalexin, cefmetasol, streptomycin, gentamicin, spiramycin, erythromycin, clindamycin, tetracycline, rifampicin, chloramphenicol, fradiomycin sulfate, and ofloxacin, etc. or anti-inflammatory agents such as ibuprofen, indomethacin, ketoprofen, mefenamic acid, antipyrine, pranoprofen, ibufenac, tiaramide hydrochloride, prednizolon, dexametazon, and triamcinolone acetonide, etc., but the desirable ingredients are not limited by these examples. Two or more agents can be combined. The amounts of the agents to be used are determined by the potency of the pharmacological actions of the agents used or the conditions of the target root canal. A manufacturing method of the present invention's formulas will be explained in detail below.

One or more kinds of water-soluble polymers, or water-insoluble or barely soluble polymers, or polymers that can be dissolved in an acidic region are dissolved in an appropriate solvent, one or more kinds of active agents that are effective for treatment of a root canal are dissolved or dispersed, and if desirable, the liquidity is adjusted, and then followed by an extrusion method. The size of the formula can be adjusted based on the size of the root canal and it is not particularly specified. Generally, it is formed in a size with a diameter ranging from 0.5 to 3.0 mm and a length ranging from 10 to 30 mm, and then cut before use based on the size and depth of the root canal where it is inserted.

As a method of using the present invention's root canal treatment agent, after cleaning the root canal and drying the pulp chamber and the root canal, a formula fitting the size of the root canal is directly inserted into the root canal, and temporarily sealed using a water-settable temporarily sealer, Cavit. The subsequent treatments are performed as usual. Although many of the drugs that are currently used are highly irritable, since the present invention's formula is a solid formula, there is barely any danger when it is used unlike the cases when handling liquid agents. In addition, it is possible to control release of the drugs by combining water-soluble polymers, or water-insoluble polymers or barely soluble polymers or polymer bases that can be dissolved in an acidic region so that an excellent slow-releasing effect can be achieved.

As mentioned above, the formulas concerned in the present invention are very useful drugs from the aspects of efficacy, safety and simplicity in application. This invention will be explained in detail below with reference to the examples, but this invention will not be limited by these examples.

(EXAMPLE OF EMBODIMENT 1)

Carboxy methyl ethyl cellulose (70 parts), triacetin (30 parts), and sodium ampicillin (5 parts) were blended uniformly. A small amount of ethanol was added and the blend was formed in a rod shape by an extrusion method. After drying, a rod-shape formula with a diameter of 1.0 mm was obtained.

(EXAMPLE OF EMBODIMENT 2)

Hydroxyl propyl cellulose (80 parts), phenol (10 parts), thymol (10 parts), and dl-menthol (5 parts) were combined and a small amount of water was added. The blend was molded by molten extrusion method to obtain a fiber-shaped formula with a diameter of 0.5 mm.

(EXAMPLE OF EMBODIMENT 3)

Ethyl cellulose (10 parts), polyethylene oxide (70 parts) and ibuprofen (5 parts) were dissolved in methylene chloride (1000 parts). A rod-shaped formula with a diameter of 1.0 mm was obtained by an extrusion method.

(EXAMPLE OF EMBODIMENT 4)

Methacrylic acid/methyl methacrylate copolymer (molar ratio: 1:1) (80 parts) was dissolved in ethanol (1000 parts). Triacetin (20 parts) and tetracycline hydrochloride (60 parts) were then added to be dissolved. The blend was molded by an extrusion method to obtain a fiber-shaped formula with a diameter of 0.3 mm.

(EXAMPLE OF EMBODIMENT 5)

Ethyl methacrylate/chlorotrimethylammonium ethyl methacrylate copolymer (molar ratio: 1:20) (10 parts) was dissolved in ethanol (1000 parts) and triacetin (2 parts) and dexametazon (2 parts) were added. The blend was molded by an extrusion method to obtain a rod-shaped formula with a diameter of 1.0 mm.

(EXPERIMENTAL EXAMPLE)

The case of insertion of the present invention's formula in the root canal of the extracted tooth and the case when an aqueous solution containing the same agents as the ingredients of the present formula was filled were compared over time with respect to the concentration of the drugs in the solution in the root canal.

Twenty four upper jar canines extracted from healthy humans for correction of malpositioned dentition were provided. All specimens were cut from the enamel and the root canal was cleaned by extirpation of the dental pulp. The formula prepared in Example of Embodiment 1 with a length of 5 mm (containing sodium ampicillin 180 μg) was inserted into each root canal of twelve canines and temporarily sealed with temporary sealer, Cavit. As controls, each root canal of the remaining 12 canines was filled with 9 μl of 2% aqueous sodium ampicillin solution (containing sodium ampicillin 180 μg) and then sealed with Cavit. Each was immersed in a phosphoric acid buffer (100 ml) at pH 7.2 at 37°C. The temporary sealing was removed on the 1st day, 3rd day, 5th day and 7th day after immersion for 3 specimens at a time and the solution in the root canal (2 μl each) was sampled with a micro syringe and the concentration of sodium ampicillin in the solution of the root canal was measured by the agar-agar flat plate diffusion method using *Streptococcus aureus* 209 P strain.

When the formula of the present invention was inserted in the root canal, the concentrations of sodium ampicillin in the solution in the root canal were as follows: 95.2 ± 3.4 μg/ml on the 1st day after immersion, 85.6 ± 6.3 μg/ml on the 3rd day after immersion, 87.4± 5.1 μg/ml on the 5th day after immersion, and 83.9 ± 6.2 μg/ml on the 7th day after immersion, indicating almost a constant level during the period from the 1st day through the 7th day. In contrast, in the case when the root canal was filled with an aqueous sodium ampicillin solution, the concentration of sodium ampicillin in the solution in the root canal was 28.6 ± 5.8 μg/ml on the 1st day after immersion, but it was below the detection limit on the 3rd day, 5th day and 7th day (detection limit: 0.5 μg/ml).

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Amendment
To the Commissioner of the Patent Office
March 31, 1988
[illegible seal]

1. Disclosure of the Case
1987 Patent Application No. 139514

2. Title of the Invention

Root Canal Treatment Agent

3. Party Filing for the Amendment
Relationships to the Case: Patent Applicant

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5. Date Amendment filed
Voluntary

6. Subjects of Amendment
Column of "Detailed Description of the Invention" in the Specification

[Stamp: April 1, 1987, illegible]

7. Contents of Amendment

(1) In line 12 of page 2, revise "entrance of the root canal" to "apical foramen."
(2) In line 23 of page 2, insert "current preferably" before "most often used."
(3) In line 25 of page 2, revise "phenol agents" to "liquid agents such as phenol agents."
(4) In line 28 of page 2, insert the following text after "one must pay special attention not to adhere them on other parts of the soft tissue in the mouth":
"Moreover, since the tip of the root canal is opened to the alveolar socket as apical foramen, even though a liquid agent is simply sealed in the root canal by temporary sealing, the agent is rapidly shifted into the tissue so that it is difficult to maintain the agent at an effective concentration in the root canal. In addition, the rapid migration of the agent may cause a hypersensitive reaction."
(5) In line 29 of page 2, revise the section from "As was mentioned above" to "remain locally at least during the active period" as follows: "From the problems mentioned above, there has been a demand for a root canal treatment agent with high safety that can be applied by a simple method. Also, a root canal treatment agent with excellent slow-release effect is necessary in order to maintain an effective concentration of the agent in the root canal at least during the active period."

End